

Abstracts

These selected abstracts and titles from the world literature are arranged in the following sections:

Syphilis and other treponematoses

(Clinical and therapy; serology and biological false positive phenomenon; pathology and experimental)

Gonorrhoea

(Clinical; microbiology; therapy)

Non-specific genital infection

Reiter's disease

Trichomoniasis

Candidosis

Genital herpes

Other sexually transmitted diseases

Public health and social aspects

Miscellaneous

Syphilis and other treponematoses (Clinical and therapy)

The incidence of treponemal disease in adult men at Loitokitok, Kajiado District

J. D. GATENBY DAVIS AND C. HINREINER (1977). *East African Medical Journal*, 54, 273-275

Sera were collected from 148 adult males, aged between 18 and 48 years, who attended the Loitokitok Hospital in the Kajiado District of southern Kenya. VDRL and TPHA tests were performed; 11 sera were reactive in both tests and 12 sera were reactive in the TPHA test only. FTA-ABS tests were positive on all, so that serological evidence of treponemal infection was present in 15.4% of the patients surveyed. Reactivity was equally divided between patients of the pastoral group of Masai and the non-pastoral Bantu. The patients were not examined, nor were histories taken, so that it was not known whether the results reflected venereal syphilis or the endemic non-venereal form. The simplicity and specificity of the TPHA test make it of especial value in epidemiological surveys of this kind.

A. E. Wilkinson

[Reprinted from *Abstracts on Hygiene*, by permission of the Editor,]

Return to normal of Argyll-Robertson pupils after treatment

F. M. LANIGAN-O'KEEFE (1977). *British Medical Journal*, 2, 1191-1192

Syphilis (Serology and biological false positive phenomenon)

Rapid detection of specific antitreponemal antibodies by counterimmunoelectrophoresis using an extract of *Treponema pallidum*

R. GHINSBERG, B. W. GRUNBAUM, AND G. BLUMSTEIN (1977). *Israel Journal of Medical Sciences*, 13, 557-560

The antigen was prepared by ultrasonic disruption of a suspension containing 10^7 *Treponema pallidum* per ml in 0.02 mol/l phosphate buffer, pH 7.0. Wells 3 mm in diameter with 5 mm between centres were cut in 0.85% agarose gel in 0.06 mol/l barbital buffer, pH 8.2. Serum was placed in the anodal and antigen in the cathodal wells and a constant voltage of 60 V at 4 mA passed for 45 minutes.

Comparison of the *T. pallidum* counterimmunoelectrophoresis (TPCIE) and FTA-ABS tests on 400 sera from patients with suspected syphilis showed agreement in 96%. Of the 16 sera which gave discrepant results the TPCIE test was positive in four and the FTA-ABS test in 12; syphilis was diagnosed on clinical grounds in 15 of these patients. In a comparison of the TPCIE and Reiter protein complement-fixation tests on 400 additional sera the results agreed in 86%. In tests on sera from 17 patients with untreated early (nine) or latent (eight) syphilis the FTA-ABS test was positive in all, the TPCIE in 14, and the RPCFT in 10. Thirty-nine sera which were thought to have given false positive RPCF results

were all negative with the FTA-ABS and TPCIE tests. The TPCIE test is thought to offer the advantages of speed, simplicity, and economy over the FTA-ABS test but to be slightly less sensitive in the detection of primary syphilis.

A. E. Wilkinson

Syphilis (Pathology and experimental)

Parasitism by virulent *Treponema pallidum* of host cell surfaces

N. S. HAYES, K. E. MUSE, A. M. COLLIER, AND J. B. BASEMA (1977). *Infection and Immunity*, 17, 184-186

The attachment of *Treponema pallidum* was four times higher for monolayers of rabbit testicular cells than for one specified line of human epithelial cells. There was greater cellular adherence when incubated at 37°C than at 33°C, 25°C, or 4°C and the effect was dependent on the quantity of added treponemes. At the most, two hours were necessary for maximal attachment. Once attached, the treponemes remained motile, but were anchored by a 'terminal tapered structure'. Exposure of cell cultures to 7000-8000 rad or to the mitogens, phytohaemagglutinin, concanavalin A, or pokeweed failed to inhibit treponemal adhesion. The cell cultures were also treated with detergents, certain enzymes, and metabolic inhibitors—again without prevention of adhesion. No treponemal adherence was found to glass particles of 5-125 µm or diethylaminoethyl-Sephadex A-50 swollen beads 40-120 µm. One per cent rabbit serum or calf

serum-coated Sephadex beads likewise failed to enhance adherence.

Heat or formalin-treated treponemes failed to adhere to cell monolayers. If incubated for 21 hours at 33°C, they showed a 75% reduction in adhesion. Similarly, high doses of potassium cyanide or sodium deoxycholate and, to a lesser extent, digitonin inhibited adhesion and motility. Exclusion of calcium and magnesium ions by ethylenediaminetetraacetate implied that adhesion was not dependent on divalent cations. No cellular adhesion was shown with pathogenic 'Reiter' treponemes. Monolayer cultures with treponemes adhering to the cell surfaces were refractory to further treponemal adhesion. Fifty per cent inhibition of adhesion was produced by preincubation with rabbit sera taken 135 days after infection with *Treponema pallidum*. These sera had a fluorescent treponemal antibody—ABS titre of 3125.

[The authors imply there is a specific cellular attachment for *Treponema pallidum*. However, this suggestion would have been more convincing if the possibility of host antibody, perhaps on the surface of the spirochaete, cross-reacting with the cells in the monolayer, particularly with the rabbit testicular cells, had been excluded.]

D. J. M. Wright

Development of macrophage migration inhibition in rabbits infected with virulent *Treponema pallidum*

C. S. PAVIA, J. D. FOLDS, AND J. B. BASEMAN (1977). *Infection and Immunity*, **17**, 651–654

Terminal electron transport in *Treponema pallidum*

P. G. LYSKO AND C. D. COX (1977). *Infection and Immunity*, **16**, 885

Gonorrhoea (Clinical)

Gonorrhoea screening in male consorts of women with pelvic infection

L. C. GILSTRAP, W. P. N. HERBERT, G. CUNNINGHAM, J. C. HAUTH, AND H. G. VAN PATTEN (1977). *Journal of the American Medical Association*, **238**, 965–966

This report describes a study of men as a reservoir of gonorrhoea and of their role in pelvic infections in women. Urethral cultures were taken from 161 male contacts of 100 women with acute gonococcal pelvic inflammatory disease (PID). Positive cultures for *N. gonorrhoeae* were obtained from 63 contacts (39%), of whom 14 (22%) were asymptomatic. It was also noted that 52% of these women had at least one sexual contact from whom *N. gonorrhoeae* was isolated. A group of 69 male contacts of 46 women with non-gonococcal PID was examined. Cultures of *N. gonorrhoeae* were yielded by 10 (15%), three of whom were asymptomatic.

In view of these findings the authors rightly recommend that all male sexual contacts of women with acute PID should be examined, with cultures for *N. gonorrhoeae*.

C. S. Ratnatunga

Futility of routine culture of hysterectomy specimens for gonorrhea

S. BURROWS (1977). *American Journal of Obstetrics and Gynecology*, **129**, 339

Resistant gonococcal infection from an intrauterine contraceptive device

E. E. DASHOW AND A. S. LLORENS (1977). *American Journal of Obstetrics and Gynecology*, **129**, 230

Gonorrhoea (Microbiology)

Ultrastructural study of cervical gonorrhea

B. A. EVANS (1977). *Journal of Infectious Diseases*, **136**, 248–254

An ultrastructural examination of the squamocolumnar junction of the cervix of patients infected with *Neisseria gonorrhoeae* is described. Gonococci were found to become firmly attached to stratified squamous epithelium, a process that appeared to be initiated by activity of the cytoplasmic membrane of superficial squames. By contrast, gonococci were not found attached to, or even closely associated with, mucus-secreting columnar epithelium. Gonococcal growth, as evidenced by numbers of organisms and surface vesicle formation, appeared most

active in cervical secretions, chiefly on exfoliated squames, but also lying free. Survival after phagocytosis by polymorphonuclear leucocytes was found not to be unique to gonococci, and it is suggested that continual phagocytic recycling minimises the significance of this occurrence. It seems probable that persistence of gonorrhoea in the female depends upon the adherence of gonococci to stratified epithelium, where they are protected from phagocytosis, and the infectivity of gonorrhoea arises from the ability of gonococci to divide rapidly on the surface of exfoliated squames, from where they are released into secretions.

Author's summary

Studies on the mechanism of pathogenicity of *Neisseria gonorrhoeae*

P. NOVOTNY, J. A. SHORT, M. HUGHES, J. J. MILLER, C. SYRETT, W. H. TURNER, J. R. W. HARRIS, AND I. P. B. MACLENNAN (1977). *Journal of Medical Microbiology*, **10**, 347–365

Gonococci in pus appear in specific clusters in which they are surrounded by organelles and granules derived from the host cells in which they multiplied. These clusters have been named *infectious units* because (1) the cocci multiply within them, (2) the whole complex makes contact with epithelial cells, (3) the cocci in the units are not recognised by polymorphs as long as the coating of granules is dense enough, and (4) the cocci are probably protected against humoral defence mechanisms. During multiplication of bacteria in infectious units, soluble antigenic material is probably produced. No morphological evidence of multiplication of gonococci outside infectious units was observed in pus from patients with gonorrhoea. Attempts to reproduce typical infection units in animal models have so far failed.

The identity of the surrounding granular coating was established morphologically and with appropriate sera labelled with ¹²⁵I and horseradish peroxidase. It is proposed that the mechanism of gonococcal pathogenicity is primarily based on the internal disorganisation of the regulatory mechanism of human macrophages. A sequence of events in the infection is discussed.

The anatomical changes observed in subcutaneously implanted plastic chambers in guinea-pigs infected with gonococci may be attributable to partial interference

with the internal regulation of phagocytes. The effect of drugs on bacterial counts in the chamber cavity was studied. Under the influence of colchicine the number of colony-forming units increased 100 times within 8 hours; vinblastine was without effect. Neither of these drugs had any effect on the growth of gonococci *in vitro*. In studies by immune electron microscopy with sera from patients with gonococcal septicaemia, IgG was shown to react strongly with the gonococcal surface, free endotoxin, ring structures (pits) liberated from the lipopolysaccharide backbone and with unspecified soluble antigenic material. The detection of pilated antibodies in these sera was rare.

Authors' summary

Surface components affecting interactions between *Neisseria gonorrhoeae* and eucaryotic cells

J. SWANSON (1977).

Journal of Infectious Diseases, 136, S138-S143

Interactions of *Neisseria gonorrhoeae* with non-leucocytic eucaryotic cells including tissue culture cells (either primary or continuous lines), human sperm, and buccal mucosal cells appear to be influenced primarily by the presence or absence of pili on the bacteria. In this context, piliation enhances attachment to or association of micro-organisms with the eucaryotic cells. Pili, on the other hand, appear to reduce interaction of *N. gonorrhoeae* with mouse peritoneal macrophages. Other groups have demonstrated that pili reduce phagocytosis of gonococci by neutrophils, but in our studies this effect is secondary to that dependent on 'leucocyte-association' factor. The presence of such a factor is correlated with a particular protein found by polyacrylamide electrophoresis. Adherence among *N. gonorrhoeae* varies and results in colony forms of different colouration or aggregation characteristics. These different colouration forms correlate with the protein patterns of gonococci as found in polyacrylamide electrophoresis and also with the susceptibility of gonococci to killing by trypsin.

Author's summary

Rapid method for auxotyping multiple strains of *Neisseria gonorrhoeae*

H. B. SHORT, V. B. PLOSCOWE, J. A. WEISS, AND F. E. YOUNG (1977).

Journal of Clinical Microbiology, 6, 244

A rapid method for auxotyping strains was developed that uses microtitre plates. This miniplaque technique enables rapid identification of major auxotypes present in clinical strains. Additional growth requirements can be identified by adding individual amino-acid supplements to complete gonococcal genetic medium. Analysis of eight clones from 40 patients revealed that 10 had more than one auxotype. Deoxyribonucleic acid-mediated transformation can be used to establish whether the strains with apparently more than one auxotype are defective in the same locus in each of the involved biosynthetic pathways. Selection of more than one clone is required in precise epidemiological studies.

Authors' summary

Auxotypes and penicillin susceptibilities of *Neisseria gonorrhoeae* isolated from patients with gonorrhoea involving two or more sites

B. W. CATLIN AND P. J. PACE (1977).

Antimicrobial Agents and Chemotherapy, 12, 147-156

The auxotype and MIC of penicillin were determined for 181 isolates from different sites in 84 patients with uncomplicated gonorrhoea. Auxotypes 1, 2, and 3 comprised 27%, 36%, and 24% of the isolates, but it was also possible to distinguish strains within an auxotype by differences in their susceptibility to antibiotics. Pairs of isolates from three patients showed different auxotypes and two of these pairs showed differences in their resistance to a range of antibiotics. This suggests that these three patients were each infected by two distinct strains of gonococci. In three other patients the paired strains showed slight differences in the MIC of penicillin, but their auxotypes and degree of resistance to other antibiotics were identical. Gonococci from eight couples with uncomplicated gonorrhoea showed the same auxotype and susceptibility to penicillin.

Twenty-one isolates from multiple sites in nine patients with disseminated gonococcal infection and three of their contacts were tested. All except one strain required arginine, hypoxanthine, and uracil for growth and were very sensitive to penicillin. Strains from different sites in the individual patients and from one contact had the same auxotype and resistance to penicillin. One patient had two contacts, the isolates were alike

in their antibiotic resistance profiles and requirement for arginine, hypoxanthine, and uracil, but the strain from one contact also required thiamine pyrophosphate for growth.

The biosynthetically less competent strains requiring arginine, hypoxanthine, and uracil seem to be less well adapted to growth and survival in the oropharynx than the nutritionally less demanding strains of auxotypes 1, 2, and 3.

A. E. Wilkinson

Conjugal transfer of R. plasmids in *Neisseria gonorrhoeae*

M. ROBERTS AND S. FALKOW (1977).

Nature, 266, 630-631

The molecular weights were determined of plasmids derived from lysates of 13 strains of *N. gonorrhoeae* which showed β -lactamase activity, that is, penicillin resistance. The molecular weights were measured by comparing differences in mobility of the plasmids in agarose gel after electrophoresis and also by measuring the contour length of open circular DNA in the electron microscope. All strains contained plasmids of 2.5 megadaltons, nine Far Eastern strains had plasmids of 4.4 megadaltons in addition, while the four strains isolated in Great Britain carried plasmids of 3.2 megadaltons. In three of the Far Eastern strains a further plasmid of 24.5 megadaltons was found.

Matings were accomplished by a variation of the filter method (not published). The donor strains were: one Far Eastern strain with high and low molecular weight plasmids and two strains containing only the lower molecular weight plasmids, one from the Far East and one from Great Britain. A penicillin sensitive recipient strain of *N. gonorrhoeae* was used which, unlike the donor strains, was resistant to nalidixic acid and rifampicin but required proline. Transfer of penicillin resistance without changes in the sensitivity to other antibiotics and alteration in proline requirement occurred only in the strain containing the large 24.5 megadalton cryptic plasmid. The strain also transferred β -lactamase activity to an ampicillin-sensitive *Escherichia coli*, the β -lactamase activity being determined by the chromogenic cephalosporin substrate. The conjugal transfer of β -lactamase activity is not accompanied by the finding of the 24.5 megadalton plasmid in the

recipient strain, although the low molecular weight plasmid is present. The plasmid transfer was not affected by pancreatic DNase but no data were provided for this experiment. All the *Neisseria* whether donor or recipient exhibited non-piliated T_4 colonial morphology (T_4 colonies are not normally competent for DNA transformation). A T_1 *N. gonorrhoeae* strain showed transformation using proline dependence as a marker with bulk DNA but not plasmid DNA using Catlin defined media. Kirven and Thornsberry (1977) have also shown conjugal transfer of DNA to other strains of *Neisseria* and to *E. coli*. They also provided data for the failure of DNase to influence conjugal transfer of genetic material.

Similar independent observations have been made by Eisenstein *et al.* (1977) who demonstrated conjugal transfer of β -lactamase activity using two penicillin resistant strains of *Neisseria* to two other strains of *Neisseria*, two *E. coli*, and also to *Neisseria flava*. They also provided experimental evidence to show that there was no phage transduction by showing that sterile filtrates of *Neisseria* broth cultures derived from penicillin resistant strains failed to transfer resistance.

These experiments indicate that conjugation but not transformation or transduction is the likely means of transfer of β -lactamase activity, also that the heavy cryptic plasmid exhibits sex factor activity. The inability to find the heavy plasmid in the British or recipient strains suggests that covalent linkage with the heavy plasmid may not be necessary. The subject is reviewed by J. R. Saunders (1977) in *Nature*, 266, 586 and the paper should be read in conjunction with that by L. A. Kirven and C. Thornsberry (1977), *Antimicrobial Agents and Chemotherapy*, 11, 1004, and by B. I. Eisenstein, T. Sox, E. Biswas, E. Blackman, and P. F. Sparling (1977), *Science*, 195, 998.

D. J. M. Wright

Molecular characterisation of two beta-lactamase-specifying plasmids isolated from *Neisseria gonorrhoeae*

M. ROBERTS, L. P. ELWELL, AND S. FALCOW (1977). *Journal of Bacteriology*, 131, 557-563

Two non-conjugative gonococcal R-plasmids of molecular mass of 4.4 megadaltons and 3.2 megadaltons were studied. Both these plasmids included β -lactamase activity. The 4.4 megadalton plasmid was originally derived from a Far Eastern

strain of *N. gonorrhoeae* while the 3.2 megadalton plasmid originated from the United Kingdom. The guanine-plus-cytosine content of these plasmids approximated to the 0.4 mol fraction. It was suggested that this value was significantly different from the guanine-plus-cytosine content of the gonococcal chromosomal deoxyribonucleic acid or of the 'indigenous' 24.5 megadalton or 2.4 megadalton plasmids. This in turn indicated that both the β -lactamase associated plasmids were not a product of a transpositional event. However, their similarity to the 4.1 megadalton plasmid derived from the β -lactamase producing strain of *Haemophilus parainfluenzae* was reinforced by the finding of a common core of deoxyribonucleic acid—deoxyribonucleic acid polynucleotide sequence of 64 to 70% of whole cell extracts of the appropriate *N. gonorrhoeae* strain, *E. coli* transformants containing the neisserial β -lactamase associated R-plasmids and an *H. influenzae* transformant containing the *H. parainfluenzae* β -lactamase R-plasmid. It was further suggested that the gonococcal R-plasmids are not necessarily derived from the *Haemophilus* species, but since they may be transformed into *E. coli* and contain 34 to 40% of the transposable *E. coli* deoxyribonucleic acid sequence TN2, the structural gene of the ubiquitous TEM β -lactamases, the β -lactamase plasmids, are derived from the enteric pool. The implication is that there has been an R-plasmid intrusion across a previously invulnerable biological barrier protecting *Neisseria* and *Haemophilus*. The appearance of β -lactamase gonococcal R-plasmids with different molecular masses presumably arose from a 1.2 megadalton deletion of a 4.4 megadalton R-plasmid.

In vitro removal of selective antibiotic pressure on gonococcal R-plasmid *E. coli* transformants showed a 45% loss of 4.4 megadalton plasmid at 60 hours, which was stable thereafter, but a 99.9% loss at 120 hours of the 3.2 megadalton plasmid. This parallels the slight increase in plasmid loss in clinical isolates of penicillin-resistant strains of *N. gonorrhoeae* from the United Kingdom (36 to 99.9% loss) whereas the Far Eastern strains showed a 30 to 98% loss. This in part may reflect that the United Kingdom isolates were collected early in the epidemic. It is interesting to speculate what effect the conjugative 24.5 megadalton plasmid has on the possible host parasite relationship in man, as this plasmid occurs in 50% of

the penicillin-resistant strains of *Neisseria gonorrhoeae* as compared with only 5% of sensitive strains.

D. J. M. Wright

Rapid penicillinase paper strip test for detection of beta-lactamase-producing *Haemophilus influenzae* and *Neisseria gonorrhoeae*

J. H. JORGENSEN, J. C. LEE, AND G. A. ALEXANDER (1977).

Antimicrobial Agents and Chemotherapy, 11, 1087-1088

Strips of Whatman filter paper no. 3 about 5 by 1 cm in size are immersed in a solution of 0.2% soluble starch (BBL) and 1% potassium penicillin G, dried at room temperature for 2 hours and stored at -20°C ; they remain stable for at least a year.

For testing, a strip is placed in a sterile Petri dish, moistened with Gram's or Lugol's iodine and the excess poured off. Growth from about 10 colonies is smeared on the strip in an area about 5 mm in diameter. If β -lactamase is produced, the dark purple colour of the strip becomes white round the area inoculated within a minute; this is due to the production of penicilloic acid which converts iodine to iodide. In a negative test the strip remains purple or becomes slightly yellow at the site of inoculation.

The test gave satisfactory results with 100 isolates of *Haemophilus influenzae* and 27 of *Neisseria gonorrhoeae*.

A. E. Wilkinson

Evidence for two distinct types of penicillinase-producing *Neisseria gonorrhoeae*

P. L. PERINE, W. SCHALLA, M. S. SIEGEL, C. THORNSBERRY, J. BIDDLE, K-H WONG, AND S. E. THOMPSON (1977). *Lancet*, 2, 993-995

Since their recognition early in 1976, penicillinase—(β -lactamase) producing *Neisseria gonorrhoeae* (PPNG) have been isolated in more than 15 countries. Most strains isolated in or epidemiologically linked with the Far East are relatively resistant to tetracycline *in vitro*, are phenotypically wild-type or proline-dependent auxotypes, and carry a plasmid with a molecular weight of 5.8 megadaltons coding for β -lactamase production. In contrast, PPNG epidemiologically

linked with West Africa are more susceptible to tetracycline, require arginine for growth, and their gene coding for β -lactamase synthesis is contained in a smaller 3.2 megadalton plasmid. Moreover, 43% of the Far Eastern strains, but none of those from West Africa, have an additional 24.5 megadalton conjugative plasmid which transfers the β -lactamase R factor(s) to other gonococci. The presence of this conjugative plasmid may explain the relatively high prevalence of PPNG in certain areas of the Far East.

Authors' summary

Penicillin sensitivity and serum resistance are independent attributes of strains of *Neisseria gonorrhoeae* causing disseminated gonococcal infection

B. I. EISENSTEIN, T. J. LEE, and P. F. SPARLING (1977).
Infection and Immunity, **15**, 834-870

This is the most comprehensive study yet to examine the inter-relationship between various phenotypic characteristics of *Neisseria gonorrhoeae* and its virulence as manifest by disseminated infection (DGI). The authors set out with the plausible hypothesis that mutation to antibiotic resistance, or adaptation from the 'wild type', might be expected to correlate with decreasing virulence. High correlations are demonstrated independently both with penicillin sensitivity (Pen^S) and resistance to the bactericidal effect of pooled human serum (serum^R). Recent reports attributing a high percentage of DGI cases to strains of gonococci with particular nutritional requirements (auxotype AHU⁻) are explained by this strain usually being penicillin sensitive, rather than by any inherent mutational effect of nutritional requirement on virulence. As regards the correlation of antibiotic sensitivity and serum resistance with virulence, the authors draw on support from other workers reporting similar phenomena in enteric bacteria, and note that all these properties are likely to be related to the bacterial surface.

Finally, the increasing prevalence of AHU⁻ strains in uncomplicated gonorrhoea is suggested as being due to the slow growing nature reported by Morello *et al.* (1976), which renders them unaffected by short-acting high levels of antibiotic as are currently in vogue for treatment.

*Sensitivity to streptomycin (Str^S) and toxic agar (Toxic agar^S) bore no significant

relationship to virulence, but there was a correlation with strains of intermediate sensitivity to erythromycin (Ery^{WT}), which comprise the 'wild types', those above and below often being genetic mutants.

Brian Evans

Protection against infection with *Neisseria gonorrhoeae* by immunization with outer membrane protein complex and purified pili

T. M. BUCHANAN, W. A. PEARCE, G. K. SCHOOLNIK, AND R. J. ARKO (1977).
Journal of Infectious Diseases, **136**, Supplement, 132-137

Some of the antigens that are capable of producing strain-related immunity to gonococcal infection in the guinea-pig are located on the outer membrane of *Neisseria gonorrhoeae*. This finding has been demonstrated by immunisation of guinea-pigs with isolated outer membranes from two different strains of *N. gonorrhoeae* prior to challenge. Isolated principal outer membrane protein complex proved a better protective immunogen than purified pili from the same strain of *N. gonorrhoeae*. Principal outer membrane protein appears to react in antibody-complement-mediated killing of gonococci, whereas antibodies to pili are only weakly bactericidal. Pili-mediated attachment of *N. gonorrhoeae* to human cells is inhibited by antibodies to pili, and maximal inhibition occurs when antibodies are directed at pili antigenically identical with the pili mediating the attachment.

Authors' summary

Immunity to gonococcal infection induced by vaccination with isolated outer membranes of *Neisseria gonorrhoeae* in guinea-pigs

T. M. BUCHANAN AND R. J. ARKO (1977).
Journal of Infectious Diseases, **135**, 879-887

Purified outer membranes from *Neisseria gonorrhoeae* strain M or B were prepared. Gonococcal outer membranes were pure as evidenced by banding in sucrose gradients at a density of 1.23 g/cm³, simple protein composition patterns when analysed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, low succinic dehydrogenase levels, and few precipitin peaks obtained in two-dimensional immunoelectrophoresis against hy-

perimmune serum to gonococcal sonicates. Isolated outer membranes administered as antigen to guinea-pigs produced strain-related protection against gonococcal infection in amounts <1% of the weight of whole gonococci required to produce comparable protection in chimpanzees. One-hundred per cent (18 of 18) and 95% of control guinea-pigs (19 of 20) were infected when challenged with M and B strain gonococci respectively. In contrast, 26% (eight of 31) and 94% (16 of 17) of guinea-pigs immunised with M strain outer membrane were infected when challenged with comparable inocula of M and B strain gonococci respectively. Similarly, 25% (two of eight) and 100% (six of six) of animals immunised with B strain outer membrane were infected when challenged with comparable inocula of B and M strain gonococci respectively. These results suggest that antigens capable of inducing strain-related protection to gonococcal infection are present within the gonococcal outer membrane.

Authors' summary

Imferon agar: improved medium for isolation of pathogenic *Neisseria*

S. M. PAYNE AND R. A. FINKELSTEIN (1977).
Journal of Clinical Microbiology, **6**, 293-297

Cell envelope of *Neisseria gonorrhoeae*: relationship between autolysis in buffer and the hydrolysis of peptidoglycan

W. S. WEGENER, B. H. HEBELER, AND S. A. MORSE (1977).
Infection and Immunity, **18**, 210-225

Radiometric detection of carbohydrate catabolism by pathogenic *Neisseria*

F. R. COX, M. E. COX, J. R. MARTIN, AND U. H. STÖER (1977).
Journal of Clinical Microbiology, **6**, 310-311

Inhibitory action of fatty acids on the growth of *Neisseria gonorrhoeae*

R. D. MILLER, K. E. BROWN, AND S. A. MORSE (1977).
Infection and Immunity, **17**, 303-318

Reversion of Kellogg's colonial types of *Neisseria gonorrhoeae* in liquid medium

S. HAFIZ, M. G. MCENTEGART, AND A. E. JEPHCOTT (1977).
Medical Microbiology, **10**, 377-380

Virulence and immunogenicity of Types 1 and 3 *Neisseria gonorrhoeae* in guinea-pig subcutaneous chambers

R. J. ARKO, K. H. WONG, S. E. THOMPSON, W. O. SCHALLA, AND L. C. LOGAN (1977). *Canadian Journal of Microbiology*, **23**, 1261-1265

β -Lactamase producing gonococcus from Ghana

J. BARROW AND I. PHILLIPS (Letter) (1977). *Lancet*, **2**, 1023

Purification of *Neisseria gonorrhoeae* surface I-antigen

N. C. CHEN, K. KAMEI, J. ZUCKERMAN, AND H. A. GAAFER (1977). *Infection and Immunity*, **18**, 230

Immunity to gonococcal infection induced by vaccination with isolated outer membranes of *Neisseria gonorrhoeae* in guinea-pigs

T. M. BUCHANAN AND R. J. ARKO (1977). *Journal of Infectious Diseases*, **135**, 879-887

A vaccine against gonorrhoea? (Leading Article) (1977). *British Medical Journal*, **2, 917.**

Perihepatitis and hepatitis as complications of experimental endocarditis due to *Neisseria gonorrhoeae* in the rabbit

R. L. KASPAR AND D. J. DRUTZ (1977). *Journal of Infectious Diseases*, **136**, 37-42

Gonorrhoea (Therapy)

Treatment of gonorrhoea with trimethoprim-sulphamethoxazole

W. C. ELLIOTT, G. REYNOLDS, C. THORNSBERRY, D. S. KELLOGG, H. W. JAFFE, S. T. BROWN, J. ARMSTRONG, AND M. E. REIN (1977). *Journal of Infectious Diseases*, **135**, 939-943

Two single-day treatment regimens of trimethoprim-sulphamethoxazole (TMP-SMZ) were compared with the standard penicillin regimen recommended by the US Public Health Service in the treatment of 271 men with uncomplicated gonococcal urethritis.

A group of 86 men received a single dose of nine tablets of TMP-SMZ (TMP-SMZ-9), 94 received 12 tablets of TMP-SMZ in two doses of six tablets at six-hourly intervals (TMP-SMZ-12), and 91 received 4.8 megaunits of aqueous procaine penicillin G intramuscularly with 1 g probenecid given orally (APPG). Patients were asked to return after 3-6 days for re-examination and further cultures for *N. gonorrhoeae*. A positive culture was considered to indicate treatment failure, regardless of a history of re-exposure to infection. Patients not returning for examination within 13 days were excluded from statistical analysis.

Failure rates were 15/66 (23%) with 20 defaulters in the TMP-SMZ-9 group, 14/74 (19%) with 20 defaulters in the TMP-SMZ-12 group, and 2/55 (4%) with 36 defaulters in the APPG group. The smaller number of defaulters in the TMP-SMZ groups is explained by the higher failure rate and therefore the persistence of symptoms.

MIC studies showed an association between the MICs of TMP, SMZ, TMP-SMZ, and penicillin. Gonococcal isolates from patients whose treatment with penicillin had failed showed increased MICs to penicillin and tetracycline. Retreatment of these patients with TMP-SMZ could result in even higher failure rates than those observed in this study, and therefore the drug should not be used in patients showing failures to penicillin or tetracycline.

One-day regimens of TMP-SMZ are unacceptable; higher doses might give better results, but are associated with increased side effects.

N. A. Durham

Spectinomycin-resistant *Neisseria gonorrhoeae*

C. THORNSBERRY, H. JAFFEE, T. BROWN, T. EDWARDS, J. W. BIDDLE, AND S. E. THOMPSON (1977). *Journal of the American Medical Association*, **237**, 2405-2406

A 26-year-old man with a urethral discharge was treated with 3.5 g ampicillin and 1 g probenecid orally without benefit. At his next visit five days later he received 2 g spectinomycin intramuscularly and again three days later. Although he was symptom-free at his next attendance four days later, his urethral smear still showed diplococci so he was given a further 2 g spectinomycin and started on a course of

tetracycline totalling 9.5 g. Swabs from the urethra, rectum, and pharynx were negative on two visits after treatment was completed. The gonococcus isolated before treatment was started was found to grow in the presence of 2048 μ g/ml spectinomycin hydrochloride but showed no cross-resistance with aminoglycosides and its sensitivity to other antibiotics was in no way exceptional. The authors found no evidence that this strain inactivated spectinomycin and conclude that its resistance was due to chromosomal mutation.

Pamela M. Waterworth

Comparison of erythromycin base and estolate in gonococcal urethritis

S. T. BROWN, A. H. B. PEDERSEN, AND K. K. HOLMES (1977). *Journal of the American Medical Association*, **238**, 1371-1373

Erythromycin base and erythromycin estolate were compared double-blind in a randomised trial in which 152 men with urethral gonorrhoea were given 1.5 g immediately, followed by 0.5 g four times a day for four days to a total of 9 g. This treatment failed to cure 23% of the base group and 24% of the estolate group, despite the mean serum erythromycin activity being nearly twice as high in the latter group. Gastrointestinal side effects occurred in 73% and 57% of cases respectively, but no evidence of hepatic dysfunction was found although enzymes were measured.

Erythromycin appears to have no place in the treatment of gonorrhoea today.

Brian Evans

***In vitro* activity of p-hydroxybenzyl penicillin (penicillin X) and five other penicillins against *Neisseria gonorrhoeae*. Comparisons of strains from patients with uncomplicated infections and from women with pelvic inflammatory disease**
S. G. SACKEL, S. ALPERT, B. ROSNER, W. MCCORMACK, AND M. FINLAND (1977). *Antimicrobial Agents and Chemotherapy*, **12**, 31-36

Minimum inhibitory concentrations (MICs) of six penicillins against 95 strains of *Neisseria gonorrhoeae* from patients with uncomplicated anogenital infections and 22 strains from women with pelvic inflammatory disease were determined by an agar plate dilution method, using an

inocula replicator. Against all 117 strains, the order of activity observed was: BL-P1654 > penicillin X > penicillin G > ampicillin > amoxicillin = carbenicillin. MICs against strains isolated from women with gonococcal pelvic inflammatory disease were significantly higher than those against isolates from uncomplicated infections: BL-P1654, $P < 0.001$; penicillin X, $P < 0.001$; penicillin G, $P < 0.001$; ampicillin, $P < 0.001$; and amoxicillin, $P < 0.05$. MICs of penicillin G were $> 0.125 \mu\text{g/ml}$ against 33 (36%) of the 92 strains from patients with uncomplicated infections, as contrasted with 15 (68%) of the 22 isolates from women with pelvic inflammatory disease ($P < 0.01$). The means of the MICs of penicillin G were $0.06 \mu\text{g/ml}$ for the former and $0.14 \mu\text{g/ml}$ for the latter.

Authors' summary

Non-specific genital infection

Early detection of chlamydial inclusions combining the use of cycloheximide-treated McCoy cells and immunofluorescence staining

B. J. THOMAS, R. T. EVANS, G. R. HUTCHINSON, AND D. TAYLOR-ROBINSON (1977). *Journal of Clinical Microbiology*, **6**, 285-292

Detection of *Chlamydia trachomatis* inclusions only 21 hours after a specimen reaches the laboratory has been achieved by the combined use of cycloheximide-treated McCoy cells and immunofluorescence staining. Moreover, cells exposed to cycloheximide were more sensitive for detecting chlamydial inclusions than those pretreated by irradiation, since larger numbers of inclusions were found in the former cells. The application of this rapid and sensitive method allows a diagnosis of chlamydial infection to be made before antibiotic therapy is started. In this way, it should enable the treatment of non-specific genital infections to be placed on a more rational basis.

Authors' summary

Survival of chlamydiae after cooling to -196°C

M. J. PRENTICE AND J. FARRANT (1977). *Journal of Clinical Microbiology*, **6**, 4-9

Factors influencing the survival of chlamydiae after freezing were re-examined. From the data presented, it is suggested that preservation of laboratory-grown chlamydiae is best achieved through the use of sucrose as the cryoprotective agent, in the presence of 10% serum. Dimethyl sulfoxide and glycerol are more toxic. The period of exposure to sucrose before freezing must be kept as short as possible and be at 4°C rather than at room temperature. The rate of cooling during freezing in sucrose is not important; however, cooling at a rate slower than 1°C/min should be avoided. Since chlamydial survival is increased by rapid thawing, the volume of the sample should be kept to a minimum. Thawed suspensions should be inoculated on to cell monolayers without delay. The application of these methods may increase the proportion of stored clinical specimens in which chlamydiae can be found.

Authors' summary

Modification of the microimmunofluorescence test to provide a routine serodiagnostic test for chlamydial infection

J. D. TREHARNE, S. DAROUGAR, AND B. R. JONES (1977). *Journal of Clinical Pathology*, **30**, 510-517

A modification of the microimmunofluorescence test to provide a practicable routine serodiagnostic test for detecting and characterising chlamydial infection is described which uses four antigen pools, one of which corresponds with each of the four main clinical and epidemiological types of chlamydial infection. The three subgroup A *Chlamydia* (*Chlamydia trachomatis*) pools are: pool 1, hyperendemic trachoma TRIC agent serotypes A, B, and C; pool 2, paratrachoma TRIC agent serotypes D, E, F, G, H, I, and K; pool 3, lymphogranuloma venereum (LGV) agent serotypes L1, L2, and L3. Pool 4 contained four representative isolates of subgroup B *Chlamydia* (*Chlamydia psittaci*).

For routine purposes sera need be screened only against these four representative antigen pools. This will detect antibody and indicate which clinical and epidemiological type of chlamydial infection is implicated, thereby clearly distinguishing those infections that are due to *C. psittaci*. The pattern of the

cross-reactions may indicate the individual serotype involved, and further titration requiring a maximum of four individual antigens is sufficient to determine the serotype. The slight loss in sensitivity (twofold) is more than compensated for by the reduction in cost and the tenfold increase in the total number of sera which can be examined.

Authors' summary

Treatment of patients suffering from chlamydial infections

E. M. C. DUNLOP (1977). *Journal of Antimicrobial Chemotherapy*, **3**, 377-380

Chlamydial, gonococcal, and herpes virus infections in neonates

G. W. CSONKA AND E. D. COUFALIK (1977). *Postgraduate Medical Journal*, **53**, 592-594

Chlamydial infections of the eye (Leading Article) (1977). *Lancet*, **2**, 857-858

Morphology and ultrastructure of *Ureaplasma urealyticum* in agar growth

F. T. BLACK AND O. VINSTER (1977). *Acta pathologica et microbiologica Scandinavica*, **85**, 281-285

Effect of urea concentration on growth of *Ureaplasma urealyticum* (T-strain mycoplasma)

G. E. KENNY AND F. O. CARTWRIGHT (1977). *Journal of Bacteriology*, **132**, 144-158

Immunological analysis of plasma membranes of a T-strain of mycoplasma (*Ureaplasma urealyticum*)

N. ROMANO, R. LA LICATA, AND G. SCARLATE (1977). *Infection and Immunity*, **16**, 734

Trichomoniasis

The influence of antimetabolites on *Trichomonas vaginalis* as an experimental model

C. P. CHRISTOW (1976). *Microbios*, **17**, 87-92

Candidosis

Kinetics of phagocytosis and intracellular killing of *Candida albicans* by human granulocytes and monocytes

P. C. J. LEIJH, M. T. VAN DEN BARSELAAR, AND R. VAN FURTH (1977). *Infection and Immunity*, **17**, 313-324

Comparative susceptibility of *Candida albicans* to amphotericin B and amphotericin B methyl ester

R. M. BANNATYNE AND R. CHEUNG (1977). *Antimicrobial Agents and Chemotherapy*, **12**, 449-454

Genital herpes

Non-venereal sclerosing lymphangitis of the penis following herpes progenitalis

W. J. B. M. AN DE STAAK (1977). *British Journal of Dermatology*, **96**, 679-684

Genital herpes and Type 1 *Herpesvirus hominis*

T. W. CHANG (1977). *Journal of the American Medical Association*, **238**, 155

Techniques for typing *Herpesvirus hominis* antibody: a comparison of inhibition of peroxidase-labelled antibody staining with inhibition of indirect haemagglutination and with micro-neutralisation

G. GERNA AND R. W. CHAMBERS (1977). *Journal of Medical Microbiology*, **10**, 309-316

Some properties of recombinants between Type 1 and Type 2 herpes simplex viruses

I. W. HALLIBURTON, R. E. RANDALL, R. A. KILLINGTON, AND D. H. WATSON (1977). *Journal of General Virology*, **36**, 471-484

Elisa for herpes simplex virus Type 2 antibodies (Letter)

P. C. GRAUBALLE AND B. F. VESTERGAARD (1977). *Lancet*, **2**, 1038-1039

Radioimmunoassay of herpes simplex virus antibody. Correlation with ganglionic infection

B. FORGHANI, T. KLASSEN, AND J. R. BARINGER (1977). *Journal of General Virology*, **36**, 371-376

Failure of levamisole in herpes simplex (Letter)

K. A. MEHR AND L. ALBANO (1977). *Lancet*, **2**, 773-774

Other sexually transmitted diseases

Venereal warts v. Bowen disease

A. LUPULESCU, A. H. MEHREGAN, H. RAHBARI, H. PINKUS, AND D. J. BIRMINGHAM (1977). *Journal of the American Medical Association*, **237**, 2520-2522

Verrucous growths of the genitalia in young patients are usually condylomata acuminata. In five cases this type of genital lesion, viewed by light microscopy, showed dysplastic cellular changes of Bowen disease, a diagnosis that was further confirmed by electron microscopy. Bowen disease should be included in the differential diagnosis of verrucous lesions of genitalia in young people and should be ruled out by histological examination.

Authors' summary

Condyloma acuminatum and squamous carcinoma of the vulva

R. M. RHATIGAN AND R. O. SAFFOS (1977). *Southern Medical Journal*, **70**, 591-594

The association of condyloma acuminatum and squamous carcinoma of the vulva in three cases, and condyloma followed by squamous dysplasia in a fourth, is reported. This association has previously been reported in both male and female genitalia and in the perineal area. In our four cases, cancer or squamous dysplasia followed long-standing or extensive condyloma, but there was no evidence of transformation from condyloma to carcinoma. In one of the cases, areas of squamous dysplasia occurred in multiple foci within a large condyloma. It is not known whether condyloma acuminatum is a precancerous skin lesion, but long-standing or extensive condylomas should alert the physician to the possibility of carcinoma.

Authors' summary

Molluscum contagiosum venereum in a women's outpatient clinic: a venereally transmitted disease

J. K. WILKIN (1977). *American Journal of Obstetrics and Gynecology*, **128**, 531-535

Molluscum contagiosum in a perigenital distribution was noted in 14 female patients who were attending a gynaecology/family planning clinic. The author examined the obstetric, marital, and sexual histories of these patients and concludes that the genital distribution, prevalence in the sexually active, documented association with sexually transmitted diseases such as gonorrhoea, and the presence of genital molluscum contagiosum in sexual partners indicate that this is a sexually transmitted disease.

(Although the author's conclusion may well be right, it should be mentioned that the results of contact tracing of patients with this disease are not very convincing. In the present study, two of the 14 patients claimed that their sexual partners had similar lesions, but neither of these seems to have been examined.)

J. D. Oriel

A case of chancroid

K. HARVEY, L. BISHOP, D. SILVER, AND T. JONES (1977). *Medical Journal of Australia*, **1**, 956

Miscellaneous

e Antigen among male homosexual patients

P. D. SIMMONS, M. N. ISLAM, S. KNOTT, J. E. BANATVALA, AND M. SUPRAN (1977). *British Medical Journal*, **2**, 1458

In this study from St Thomas's Hospital, London, hepatitis B surface antigen (HBsAg), e antigen and its antibody (anti-e), antibody to core antigen (anti-HBc) and the presence of Dane particles were determined in sera from a selected group of male patients.

Of 1602 patients tested 58 (3.6%) were HBsAg positive. Of 360 male homosexuals 20 (5.5%) were HBsAg positive compared with 34 (3.4%) of 993 male heterosexuals. This difference was not significant ($P > 0.05$). However, e antigen was present in the sera of nine (45%) of 20 homosexuals, but in only four (13%) of 30

heterosexuals ($P < 0.02$). There was no significant difference in the proportion of HBsAg-positive homosexual and heterosexual patients who were anti-e positive or anti-HBc positive, and similar anti-HBc titres were present in both groups.

e Antigen is thought to be a marker of hepatitis-B virus infectivity, and the importance of care in handling sera from homosexuals is stressed. The Dane particle, which is probably the virus of hepatitis-B, was detected in 10 (77%) of 13 e-antigen positive sera but in only two (25%) of 8 which contained anti-e ($P < 0.02$).

J. D. Oriel

***Corynebacterium vaginale* in women with leucorrhoea**

W. E. JOSEY, W. J. MCKENZIE, AND D. W. LAMBE (1977).

American Journal of Obstetrics and Gynecology, **126**, 574-577

The authors studied 288 patients attending the Emory University Clinic, Atlanta, Ga, in whom leucorrhoea was found on examination. Specimens were taken from the vagina and cervix for culture, and in the majority direct microscopy was performed on wet preparations of the vaginal discharge. The patients were aged between 14 and 69 years. Cultures were also obtained from a control group of 30 women with no symptoms or signs of genital tract disease.

Cultures of *C. vaginale* were obtained from 164 (56.9%) of 288 patients with leucorrhoea, but from only four (13.3%) of 30 in the control group. A subgroup of 100 patients was studied to determine the probable cause of their leucorrhoea. In 13, the cause was non-infective. Among the other 87, yeasts were recovered from 54, *T. vaginalis* from 15, and *C. vaginale* from 33.

The authors discuss the pathogenicity of *C. vaginale*. They consider the characteristic discharge to be of a pasty consistency, clinging to the vaginal wall, and with a distinctive odour. They believe that cultural methods are the only reliable diagnostic techniques, and that 'clue cells' on a wet film are of less value. They use ampicillin or cephalixin for treatment.

(Further data on these patients can be found in Epidemiological characteristics of women infected with *Corynebacterium vaginale*, W. E. Josey and D. W. Lambe

(1976). *Journal of the American Venereal Disease Association*, **3**, 9-13.)

G. D. Morrison

Evaluation of tetracycline or penicillin and ampicillin for treatment of acute pelvic inflammatory disease

F. G. CUNNINGHAM, J. C. HAUTH, J. D. STRONG, W. N. P. HERBERT, L. C. GILSTRAP, R. H. WILSON, AND S. S. KAPPUS (1977).

New England Journal of Medicine, **296**, 1380-1383

To evaluate guidelines for outpatient treatment of acute pelvic inflammatory disease recommended by the Center for Disease Control we studied 197 afflicted women. They were treated either with tetracycline hydrochloride 1.5 g immediately followed by 500 mg six-hourly for 10 days or with aqueous procaine penicillin G, 4.8 megaunits intramuscularly, with 1 g probenecid by mouth, followed by ampicillin 500 mg six-hourly for 10 days. Of the whole group, 92% were subsequently seen at least once to assess efficacy of clinical and microbiological treatment.

N. gonorrhoeae was isolated from the lower genital tract in 68% of these women, and although they had a quicker symptomatic response than those with non-gonococcal infection ($P < 0.01$), the two regimens were equally effective in producing clinical cure. However, subsequent identification of a pelvic abscess was 10 times more common in women from whom *N. gonorrhoeae* was not isolated.

Therapy for pelvic inflammatory disease must be empirical, since it is impossible to distinguish clinically between gonococcal and non-gonococcal infection, and our data indicate that both regimens recommended by the Center for Disease Control are effective.

Authors' summary

Rosamicin—a new drug for the treatment of bacterial prostatitis

A. BAUMUELLER, U. HOYME, AND P. O. MADSEN (1977).

Antimicrobial Agents and Chemotherapy, **12**, 240-242

Rosamicin, a new macrolide substance, was investigated in dogs and humans with regard to its usefulness for the treatment of bacterial prostatitis and compared with the well-known macrolide erythro-

mycin. In dogs with normal and experimentally infected prostates, concentration ratios for rosamicin in prostatic secretion, interstitial fluid (obtained from implanted tissue chambers), and tissue were significantly higher than for erythromycin. The difference was even more pronounced in human prostatic tissue, obtained by transurethral resection. With its broad spectrum against many common urinary pathogens, rosamicin seems to be a promising drug for the treatment of acute and chronic bacterial prostatitis.

Authors' summary

Rosamicin in urethral and vaginal secretions and tissues in dogs and rats

U. HOYME, A. BAUMUELLER, AND P. O. MADSEN (1977).

Antimicrobial Agents and Chemotherapy, **12**, 237-239

In animal studies we investigated the distribution of rosamicin in plasma and in urethral and vaginal tissues in rats as well as in urethral and vaginal secretions in dogs. We found concentration ratios between urethral secretion and plasma of 1.9 and between vaginal secretion and plasma of 2.4. The rosamicin concentration in urethral and vaginal tissue significantly exceeded the levels of all other tissues investigated. Because rosamicin could be valuable for the treatment of bacterial urethritis and the colonisation of the vaginal introitus with faecal bacteria in women, it should be investigated clinically in this respect.

Authors' summary

In vitro activity of rosamicin against *Neisseria* and *Haemophilus*, including penicillinase-producing strains

C. C. SANDERS AND W. E. SANDERS (1977).

Antimicrobial Agents and Chemotherapy, **12**, 293-294

Microbial flora of the vagina and cervix

C. M. CORBISHLEY (1977).

Journal of Clinical Pathology, **30**, 745-748

The bacteriology of the cervix and uterus

R. A. SPARKS, B. G. A. PURRIER, P. J. WATT, AND M. ELSTEIN (1977).

British Journal of Obstetrics and Gynaecology, **84**, 701-704

The interesting case. Fixed drug eruption due to metronidazole

R. P. C. NAIK AND G. SINGH (1977).

Dermatology, **155**, 59-60